

SUBMISSION UNDER MPEP 609 D

Page 1 of 5

|                        |                 |
|------------------------|-----------------|
| Application Number     | 10/056,828      |
| Filing Date            | 24 January 2002 |
| First Named Inventor   | PLATA SALAMAN   |
| Group Art Unit         | Not Assigned    |
| Examiner Name          | Not Assigned    |
| Attorney Docket Number | ORT-1573        |

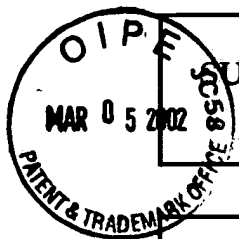
### U.S. PATENT DOCUMENTS

| Examiner Initials | Cite No. <sup>1</sup> | Name of Patentee or Applicant of Cited Document | U.S. Patent Document |                                   | Pages, Columns, Lines, where relevant passages or relevant figures appear |
|-------------------|-----------------------|---|----------------------|-----------------------------------|---|
|                   |                       |   | Number               | Kind Code <sup>2</sup> (if known) |   |
|                   |                       | Maryanoff et al.                                | US 4,513,006         |                                   | —   |
|                   |                       | Lin, Fu-Kuen                                    | US 4,703,008         |                                   | —   |
|                   |                       | Costanzo et al.                                 | US 5,242,942         |                                   | —   |
|                   |                       | Pitt et al.                                     | US 5,354,934         |                                   | —   |
|                   |                       | Costanzo et al.                                 | US 5,384,327         |                                   | —   |
|                   |                       | O'Brien, John S.                                | US 5,571,787         |                                   | —   |
|                   |                       | Martinez et al.                                 | US 5,643,575         |                                   | —   |
|                   |                       | Powell, Jerry S.                                | US 5,688,679         |                                   | —   |
|                   |                       | O'Brien et al.                                  | US 5,696,080         |                                   | —   |
|                   |                       | O'Brien, J.S.                                   | US 5,700,909         |                                   | —   |
|                   |                       | O'Brien, J.S.                                   | US 5,714,459         |                                   | —   |
|                   |                       | Shank, Richard P.                               | US 5,753,694         |                                   | —   |
|                   |                       | Johnson et al.                                  | US 5,767,078         |                                   | —   |
|                   |                       | Wrighton et al.                                 | US 5,773,569         |                                   | —   |
|                   |                       | Mehta et al.                                    | US 6,001,800         |                                   | —   |

### FOREIGN PATENT DOCUMENTS

| Examiner Initials | Cite No. <sup>1</sup> | Name of Patentee or Applicant of Cited Document | Foreign Patent Document |                     |                        | Pages, Columns, Lines, where relevant passages or relevant figures appear | T <sup>6</sup> |
|-------------------|-----------------------|---|-------------------------|---------------------|------------------------|---|----------------|
|                   |                       |   | Office <sup>3</sup>     | Number <sup>4</sup> | Kind Code <sup>5</sup> |   |                |
|                   |                       | KIRIN-AMGEN, INC.                               |                         | EPO 640619          |                        | —   |                |
|                   |                       | TRANSKARYOTIC THERAPIES, INC.                   |                         | WO 94/12650         |                        | —   |                |
|                   |                       | AMGEN, INC.                                     |                         | WO 95/03034         |                        | —   |                |
|                   |                       | JOHNSON & JOHNSON                               |                         | WO 96/40772         |                        | —   |                |
|                   |                       | ORTHO PHARMACEUTICAL CORPORATION                |                         | WO 98/00124         |                        | —   |                |
|                   |                       | ORTHO PHARMACEUTICAL CORPORATION                |                         | WO 98/05363         |                        | —   |                |
|                   |                       | BOEHRINGER MANNHEIM GMBH                        |                         | WO 99/05268         |                        | —   |                |
|                   |                       | HOECHST MARION ROUSSEL DEUTSCHLAND GMBH         |                         | WO 99/11781         |                        | —   |                |
|                   |                       | NEUROSFERES HOLDINGS, LTD.                      |                         | WO 99/21966         |                        | —   |                |
|                   |                       | BETH ISRAEL DEACONESS MEDICAL CENTER            |                         | WO 99/38890         |                        | —   |                |
|                   |                       | GENZYME TRANSGENICS CORP.                       |                         | WO 99/66054         |                        | —   |                |
|                   |                       | ORTHO-MCNEIL PHARMACEUTICAL, INC.               |                         | WO 00/61138         |                        | —   |                |
|                   |                       | KENNETH S. WARREN LABORATORIES                  |                         | WO 00/61164         |                        | —   |                |

|                    |  |                 |           |
|--------------------|--|-----------------|-----------|
| Examiner Signature |  | Date Considered | 12 Dec 02 |
|--------------------|--|-----------------|-----------|



## SUBMISSION UNDER MPEP 609 D

Page 2 of 5

|                        |               |
|------------------------|---------------|
| Application Number     | 10/056,828    |
| First Named Inventor   | PLATA SALAMAN |
| Attorney Docket Number | ORT-1573      |

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published                       | T <sup>2</sup> |
|--------------------|-----------------------|--|----------------|
|                    |                       | <u>Alafaci</u> et al., "Effect of Recombinant Human Erythropoietin on Cerebral Ischemia Following Experimental Subarachnoid Hemorrhage", <i>Eur. J. Pharmacol.</i> (2000) <b>406</b> (2):219-225.  |                |
|                    |                       | <u>Aldenkamp</u> et al., "A Multicenter, Randomized Clinical Study to Evaluate the Effect on Cognitive Function of Topiramate Compared with Valproate as Add-On Therapy to Carbamazepine in Patients with Partial-Onset Seizures", <i>Epilepsia</i> (2000) <b>41</b> (9):1167-1178   |                |
|                    |                       | William M. Armstead, "Age-Dependent Cerebral Hemodynamic Effects of Traumatic Brain Injury in Newborn and Juvenile Pigs", <i>Microcirculation</i> (2000) <b>7</b> (4):225-235.   |                |
|                    |                       | D. M. Basso, "Neuroanatomical Substrates of Functional Recovery after Experimental Spinal Cord Injury: Implications of Basic Science Research for Human Spinal Cord Injury", <i>Phys. Ther.</i> (2000) <b>80</b> (8):808-817.  |                |
|                    |                       | <u>Bernaudin</u> et al., "A Potential Role for Erythropoietin in Focal Permanent Cerebral Ischemia in Mice", <i>J. Cereb. Blood Flow Metab.</i> (1999) <b>19</b> (6):643-651.  |                |
|                    |                       | Robert F. Brady, "Cyclic Acetals of Ketoses, Part III: Re-Investigation of the Synthesis of the Isomeric <sup>D</sup> -O-isopropylidene- <sup>B</sup> -D-Fructopyranoses", <i>Carbohydrate Res.</i> (1970) <b>15</b> (1):35-40.  |                |
|                    |                       | <u>Brines</u> et al., "Erythropoietin Crosses the Blood-Brain Barrier to Protect Against Experimental Brain Injury", <i>P. N. A. S. U S A</i> (2000) <b>97</b> (19):10526-10531.   |                |
|                    |                       | Leslie A. Burton and Cynthia Harden, "Effect of Topiramate on Attention", <i>Epilepsy Res.</i> (1997) <b>27</b> (1):29-32.   |                |
|                    |                       | <u>Campana</u> et al., "Identification of a Neurotrophic Sequence of Erythropoietin", <i>Inter. J. Mol. Med.</i> (1998) <b>1</b> (1):235-241.  |                |
|                    |                       | <u>Di Giulio</u> et al., "Glycosaminoglycans Co-Administration Enhance Insulin-Like Growth Factor-I Neuroprotective and Neuroregenerative Activity in Traumatic and Genetic Models of Motor Neuron Disease: A Review", <i>Int. J. Dev. Neurosci.</i> (2000) <b>18</b> (4-5):339-346. |                |
|                    |                       | <u>Faught</u> et al., "Topiramite Dose-Ranging Trial in Refractory Partial Epilepsy", <i>Epilepsia</i> (1995) <b>36</b> (S4): pg. 33.  |                |
|                    |                       | Tracy A. Glauser, "Video Atlas of Epileptic Seizures: Classical Examples", <i>Epilepsia</i> (1999) <b>40</b> (S5):S71-80.<br>Volume 40(5) pg. 664-5.   |                |
|                    |                       | <u>Greco</u> et al., "The Search for Synergy: A Critical Review from a Response Surface Perspective", <i>Pharmacol. Rev.</i> (1995) <b>47</b> (2):331-385.   |                |
|                    |                       | Byung H. Han and David M. Holtzman, "BDNF Protects the Neonatal Brain from Hypoxic-Ischemic Injury <i>In Vivo</i> via the ERK Pathway", <i>J. Neurosci.</i> (2000) <b>20</b> (15):5775-5781.   |                |
|                    |                       | Mir Hedayatullah and Alain Guy, "Synthesis and Reduction of Aryl Azidosulfates (Synthese et Reduction d'Azidosulfates d'Aryle)", <i>Tetrahedron Lett.</i> (1975), <b>16</b> (29):2455-2458.  |                |

|                    |  |                 |           |
|--------------------|--|-----------------|-----------|
| Examiner Signature |  | Date Considered | 12 Dec 02 |
|--------------------|--|-----------------|-----------|



## SUBMISSION UNDER MPEP 609 D

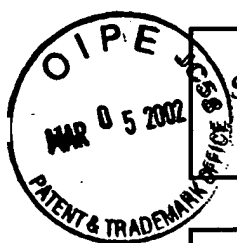
Page 3 of 5

|                        |               |
|------------------------|---------------|
| Application Number     | 10/056,828    |
| First Named Inventor   | PLATA SALAMAN |
| Attorney Docket Number | ORT-1573      |

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T <sup>2</sup> |
|--------------------|-----------------------|--|----------------|
|                    |                       | Herbert O. House, "Metal Hydride Reductions and Related Reductions", <u>Modern Synthetic Reactions</u> (Organic Chemistry Monograph Series), 2 <sup>nd</sup> Ed. (Benjamin-Cummings Publishing Co., Menlo Park, CA, 1972) pg. 45-144.                          |                |
|                    |                       | Juul et al., "Immunohistochemical Localization of Erythropoietin and its Receptors in the Developing Human Brain", <i>Pediatr. Dev. Pathol.</i> (1999) 2(2):148-158.   |                |
|                    |                       | Juul et al., Erythropoietin and Erythropoietin Receptor in the Developing Human Central Nervous System", <i>Pediatr. Res.</i> (1998) 43(1):40-49.  |                |
|                    |                       | Juul et al., "Erythropoietin in the Cerebrospinal Fluid of Neonates who Sustained CNS Injury", <i>Pediatr. Res.</i> (1999) 46(5):543-547.  |                |
|                    |                       | L. Kambova, "Recombination Erythropoietin Improves Cognitive Function in Chronic Haemodialysis Patients", <i>Nephrol. Dial. Transplant.</i> (1998) 13(1):229.  |                |
|                    |                       | Koshimura et al., "Effects of Erythropoietin on Neuronal Activity", <i>J. Neurochem.</i> (1999) 72(6):2565-2572.   |                |
|                    |                       | Sanford B. Krantz, "Erythropoietin", <i>Blood</i> (1991) 77(3): 419-434.   |                |
|                    |                       | Gerald L. Larson and Antonio Hernandez, "Reaction of Trimethylsilyl Enol Ethers with Diols", <i>J. Org. Chem.</i> (1973) 38(22):3935-3936.   |                |
|                    |                       | H. L. Laurer and T. K. McIntosh, "Experimental Models of Brain Trauma", <i>Curr. Opin. Neurol.</i> (1999) 12(6):715-721.   |                |
|                    |                       | Lee et al., "Protective Effect of Topiramate Against Hippocampal Neuronal Damage after Global Ischemia in the Gerbils", <i>Neuroscience Letters</i> (2000) 281(2-3):183-186.   |                |
|                    |                       | Maryanoff et al., "Anticonvulsant O-Alkyl Sulfamates: 2,3:4,5-Bis-O-(1-Methylethylidene)-Beta-D-Fructopyranose Sulfamate and Related Compounds", <i>J. Medicinal Chemistry</i> (1987) 30(5):880-887.   |                |
|                    |                       | Maryanoff et al., "Anticonvulsant Sugar Sulfamates: Potent Cyclic Sulfate and Cyclic Sulfite Analogues of Topiramate", <i>Bioorg. Med. Chem. Lett.</i> (1993) 3(12):2653-2656.   |                |
|                    |                       | Maryanoff et al., "Structure - Activity Studies on Anticonvulsant Sugar Sulfamates Related to Topiramate: Enhanced Potency with Cyclic Sulfate Derivatives", <i>J. Med. Chem.</i> (1998) 41(8):1315-1343.  |                |
|                    |                       | M. Mason-Garcia and B. S. Beckman, "Signal Transduction in Erythropoiesis", <i>Faseb Journal</i> (1991) 5(14): 2958-2964.  |                |
|                    |                       | Mattson et al., "Calcium, Free Radicals and Excitotoxic Neuronal Death in Primary Cell Culture", <i>Methods Cell Biol.</i> (1994) 46:187-216.  |                |
|                    |                       | Italo Mocchetti and Jean R. Wrathall, "Neurotrophic Factors In Central Nervous System Trauma", <i>J. Neurotrauma</i> (1995) 12(5):853-870.   |                |
|                    |                       | Morishita et al., "Erythropoietin Receptor is Expressed in Rat Hippocampal and Cerebral Cortical Neurons, and Erythropoietin Prevent In Vitro Glutamate-Induced Neuronal Death", <i>Neuroscience</i> (1997) 76(1):105-116.                                     |                |

|                    |  |                 |           |
|--------------------|--|-----------------|-----------|
| Examiner Signature |  | Date Considered | 12 DEC 02 |
|--------------------|--|-----------------|-----------|



|  |                        |               |
|--|------------------------|---------------|
| SUBMISSION UNDER MPEP 609 D<br>Page 4 of 5 | Application Number     | 10/056,828    |
|  | First Named Inventor   | PLATA SALAMAN |
|  | Attorney Docket Number | ORT-1573      |

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T <sup>2</sup> |
|--------------------|-----------------------|--|----------------|
|                    |                       | <u>Nakamura</u> et al., "Inhibition by Topiramate of Seizures in Spontaneously Epileptic Rats and DBA/2 Mice", <i>Eur. J. Pharmacol.</i> (1994) <b>254</b> (1-2):83-89.  |                |
|                    |                       | Newey et al., "Alternative Splicing of Dystrobrevin Regulates the Stoichiometry of Syntrophin Binding to the Dystrophin Protein Complex", <i>Curr. Biol.</i> (2000) <b>10</b> (20):1295-1298.  |                |
|                    |                       | A. R. Nissenson, "Epoetin And Cognitive Function", <i>Am. J. Kidney Dis.</i> (1992) <b>20</b> (1S1):21-24.   |                |
|                    |                       | <u>Raghupathi</u> et al., "Apoptosis After Traumatic Brain Injury", <i>J. Neurotrauma</i> (2000) <b>17</b> (10):927-938.   |                |
|                    |                       | Heikki Rauvala and H. Benjamin Peng, "HB-GAM (Heparin-Binding Growth-Associated Molecule) and Heparin-Type Glycans in the Development and Plasticity of Neuron-Target Contacts", <i>Prog. Neurobiol.</i> (1997) <b>52</b> (2):127-144.                         |                |
|                    |                       | <u>Reife</u> et al., "Topiramate as Add-On Therapy: Pooled Analysis of Randomized Controlled Trials in Adults", <i>Epilepsia</i> (2000) <b>41</b> (S1):S66-71.   |                |
|                    |                       | <u>Ronn</u> et al., "The Neural Cell Adhesion Molecule in Synaptic Plasticity and Ageing", <i>Int. J. Dev. Neurosci.</i> (2000) <b>18</b> (2-3):193-199.   |                |
|                    |                       | <u>Sachdeo</u> et al., "Topiramate: Double-Blind Trial as Monotherapy", <i>Epilepsia</i> (1995) <b>36</b> (S4): pg.33.   |                |
|                    |                       | Rajesh C. Sachdeo, "Topiramate: Clinical Profile in Epilepsy", <i>Clin. Pharmacokinet.</i> (1998) <b>34</b> (5):335-346.   |                |
|                    |                       | <u>Sadamoto</u> et al., "Erythropoietin Prevent Place Navigation Disability and Cortical Infarction in Rats with Permanent Occlusion of the Middle Cerebral Artery", <i>Biochem. Biophys. Res. Comm.</i> (1998) <b>9</b> ; <b>253</b> (1):26-32.               |                |
|                    |                       | <u>Sakanaka</u> et al., "In Vivo Evidence that Erythropoietin Protects Neurons from Ischemic Damage", <i>P.N.A.S. USA</i> (1998) <b>95</b> (8):4635-4640.  |                |
|                    |                       | Martin E. Schwab, "Experimental Aspects of Spinal Cord Regeneration", <i>Curr. Opin. Neurol. Neurosurg.</i> (1993) <b>6</b> (4):549-553.   |                |
|                    |                       | Irina Semkova and Josef Kriegstein, "Neuroprotection Mediated via Neurotrophic Factors and Induction of Neurotrophic Factors", <i>Brain Res. Rev.</i> (1999) <b>30</b> (2):176-188.  |                |
|                    |                       | <u>Shank</u> et al., "Topiramate: Preclinical Evaluation of a Structurally Novel Anticonvulsant", <i>Epilepsia</i> (1994) <b>35</b> (2):450-460.   |                |
|                    |                       | Amy D. Sinor and David A. Greenberg, "Erythropoietin Protects Cultured Cortical Neurons, but not Astroglia, from Hypoxia and AMPA Toxicity", <i>Neurosci. Lett.</i> (2000) <b>290</b> (3):213-215.   |                |
|                    |                       | <u>Smith-Swintosky</u> et al., "Topiramate Promotes Neurite Outgrowth and Recovery of Function After Nerve Injury", <i>NeuroReport</i> (2001) <b>12</b> (5):1031-1034.   |                |
|                    |                       | <u>Tabira</u> et al., "Neurotrophic Effect of Hematopoietic Cytokines on Cholinergic and Other Neurons In Vitro", <i>Int. J. Dev. Neurosci.</i> (1995) <b>13</b> (3/4):241-252.  |                |

|                    |  |                 |           |
|--------------------|--|-----------------|-----------|
| Examiner Signature |  | Date Considered | 12 Dec 02 |
|--------------------|--|-----------------|-----------|

## SUBMISSION UNDER MPEP 609 D

Page 5 of 5

Application Number

10/056,828

First Named Inventor

PLATA SALAMAN

Attorney Docket Number

ORT-1573

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate),<br>title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s),<br>volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|-----------------------|--------------------------|---|----------------|
|                       |                          | Yuji Taoka and Kenji Okajima, "Spinal Cord Injury in the Rat", <i>Prog. Neurobiol.</i> (1998) <b>56(3)</b> :341-358.  |                |
|                       |                          | Temple et al., "Recombinant Erythropoietin Improves Cognitive Function in Patients Maintained on Chronic Ambulatory Peritoneal Dialysis", <i>Nephrol. Dial. Transplant.</i> (1995) <b>10(9)</b> :1733-1738.   |                |
|                       |                          | Thompson et al., "Effects of Topiramate on Cognitive Function, <i>J. Neurol. Neurosurg. Psych.</i> (2000) <b>69(5)</b> :636-641.  |                |
|                       |                          | Tsuchiya et al., "3-Deoxygenation of Methyl $\alpha$ -D-Glucopyranosides by Treatment of Their 3- <u>O</u> .N.N -Dimethylsulfamoyl) Derivatives with Sodium Metal in Liquid Ammonia", <i>Tetrahedron Lett.</i> (1978) <b>19(36)</b> :3365-3368.                       |                |
|                       |                          | Verderio et al., "Synaptogenesis in Hippocampal Cultures", <i>Cell. Mol. Life Sci.</i> (1999) <b>55(11)</b> :1448-1462.   |                |
|                       |                          | C. S. von Bartheld, "Neurotrophins in the Developing and Regenerating Visual System", <i>Histol. Histopathol.</i> (1998) <b>13(2)</b> :437-459.   |                |
|                       |                          | Albert Wauquier and Zhou Shangdan, "Topiramate: A Potent Anticonvulsant in the Amygdala-Kindled Rat", <i>Epilepsy Research</i> (1996) <b>24(2)</b> :73-77.  |                |
|                       |                          | Yang et al., "Enhanced Neuroprotection and Reduced Hemorrhagic Incidence in Focal Cerebral Ischemia of Rat by Low Dose Combination Therapy of Urokinase and Topiramate", <i>Neuropharmacol.</i> (2000) <b>39(5)</b> :881-888.   |                |
|                       |                          | Yang et al., "Neuroprotection by Delayed Administration of Topiramate in a Rat Model of Middle Cerebral Artery Embolization", <i>Brain Res.</i> (1998) <b>804(2)</b> :169-176.  |                |
|                       |                          | Yang et al., "Usefulness of Postischemic Thrombolysis With or Without Neuroprotection in a Focal Embolic Model of Cerebral Ischemia", <i>J. Neurosurg.</i> (2000) <b>92(5)</b> :841-847.  |                |
|                       |                          | Zhang et al., "Topical Application of Neurotrophin-3 Attenuates Ischemic Brain Injury after Transient Middle Cerebral Artery Occlusion in Rats", <i>Brain Res.</i> (1999) <b>842(1)</b> :211-214.   |                |

Examiner  
SignatureDate  
Considered

12 Dec 02